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<u>Original Article</u> Clinico-radiological profile of pulmonary tuberculosis among patients of diabetes mellitus

Author

Dr Harender Singh Chaudhary

Senior Resident, Department of Respiratory Medicine, U.P.U.M.S., Saifai, Etawah, India

Abstract

Introduction: India being Diabetic Capital with largest number of tuberculosis patients. Several studies have highlighted that Diabetes as a risk factor for TB. TB in Diabetic patients tends to have more cavitatary, bilateral, multiple lobe involvement. Hence We would like to highlight the varied pulmonary manifestations through our study.

Methodology: Cross sectional study conducted at department of Respiratory Medicine, U.P.U.M.S., SAIFAI, ETAWAH with 220 patients. Pulmonary TB was diagnosed through history, examination, Sputum Microscopy and Chest X ray.

Results and Discussion: Out of 220,154(70%) males & 66(30%). Maximum incidence of TB was seen in >50 years with peak incidence in 51-60 & 61-70 years. Symptoms noted were cough(94.55%), Fever(90%), Anorexia (52.73%), Loss of weight (50.91%), Dyspnea (43.64%), Haemoptysis (21.81%), night sweats (17.27%), Chest pain(7.27%).

Sputum positive cases male (138/154) and female (54/66) with P=0.011. Cavity with nodule was present in 36.36% of patients and patients have normal chest x-ray is seen in 2.72% of patients.

Conclusions: There was a linear relationship between duration of DM & TB incidence. Majority of our patients had poorly controlled sugars, suggesting that severe hyperglycaemia is associated with development of pulmonary tuberculosis.

Lower lung field involvement was noted in 20.90% of patients. Early diagnosis and properly monitored treatment regimen is the only time proven answer.

Introduction

Since ancient times, physicians have been aware of the association between tuberculosis and diabetes mellitus: perhaps the earliest to note it was the great Indian physician Sushruta, in 600 A.D, while Avicenna (780-1027 A.D.) had commented that phthisis frequently complicated diabetes. Autopsy of diabetics in 1883 showed presence of Tubercular granuloma in 50% of diabetics. Tuberculosis and Diabetes mellitus (DM) are two major public health problems which not only often coexist but have serious implications on each other. DM has an impact on radiological symptomatology, manifestation, diagnosis and management of TB. Prior to the insulin era: Diagnosis of DM was a death Leading sentence. cause of death was: Tuberculosis. During the early 20th century, it was said that a patient with diabetes who did not die in a diabetic coma was likely to die of TB,

particularly if the patient was poor. In the early 20th century, the effect of DM on TB was large concern of investigators, but this was somewhat neglected in the second half of the 20th century with the emergence of proper treatment for both diseases.^{1,2} Tuberculosis is an infectious disease caused predominantly by Mycobacterium tuberculosis. The life time risk of developing to disease among those infected with Mycobacterium tuberculosis is 5-10%.³ Though India is the second-most populous country in the world. In 2015, out of the estimated global annual incidence of 9.6 million TB cases, 2.2 million were estimated to have occurred in India which is onefourth of the global incidence.⁴

WHO estimated burden of tuberculosis in India, 2015^4

Rate Per 1,00,000 Persons

Incidence 167 (156-179)

Prevalence 195 (131-271)

Mortality 17 (12-27)

Burden of diabetes mellitus according to International Diabetes Federation (IDF)-DIABETES ATLAS-7TH EDITION -2015

Global-415 million

642 million people by 2040

India-69 million.⁵

Association between diabetes mellitus and pulmonary tuberculosis is well established while the prevalence of tuberculosis is increased 4-5 times more among patient of Diabetes Mellitus⁶

Aim & Objectives

- 1. To study the clinical profile of pulmonary tuberculosis in Diabetic patients.
- 2. To study the radiographic pattern of pulmonary tuberculosis in Diabetic patients.

Materials and Method

Study Design

Hospital based cross-sectional study.

Sample Size: 220

Study Duration

Feb 2016-June 2017

Place of Study

Department of Respiratory Medicine, Uttar Pradesh University of Medical Sciences(UP UMS), Saifai, Etawah.

Study Sample

All the patients who were admitted in Respiratory medicine ward as a case of Pulmonary tuberculosis with Diabetes Mellitus formed the sample size.

Data Analysis

SPSS 23 version is used for data analysis. Chisquare test was used to analyse the collected data.

Ethical Consideration

The study protocol was taken from the institutional ethical committee of UPUMS, Saifai, Etawah. Before enrolment of study written informed consent from each subject was obtained in response to fully written and verbal explanation of the nature of the study.

Inclusion Criteria

- Patients with diabetes mellitus (whose Fasting plasmaglucose>126 mg/dl and/or post prandial (two hour) plasma glucose > 200 mg/dl or HbA1c >6.5%).
- 2. Patients with pulmonary tuberculosis.

Exclusion Criteria

- 1. Patient not willing to participate in study.
- 2. Tuberculosis patients not having diabetes.
- 3. Extra pulmonary tuberculosis
- 4. Patients with HIV/AIDS.
- 5. Patient under chemotherapy or radiotherapy.
- 6. Patient on prolonged steroid therapy.

Method of Collection of Data

Pulmonary tuberculosis was diagnosed by -

All patients who satisfied the above criteria were examined in detail and subjected to relevant laboratory and radiological investigations.

- Detailed history.
- Clinical examination.
- Sputum examination for acid-fast bacilli
- Chest radiography.

Diabetes mellitus was diagnosed by – WHO Diagnostic Criteria-¹⁴

Symptom of diabetes plus random blood sugar $\geq 11.1 \text{ mmol/l}$ (200 mg/dl) or Fasting plasma glucose $\geq 7.0 \text{ mmol/l}$ (126 mg/dl) or post prandial (two hour) plasma glucose $\geq 11.1 \text{ mmol/l}$ (200 mg/dl) during an oral glucose tolerance test (Anhydrous glucose 75gm).

Special Investigation

- 1. Sputum AFB
- 2. Chest X Ray
- 3. HbA1C
- 4. RBS
- 5. Fasting blood sugar
- 6. Post prandial blood sugar
- 7. HRCT-Thorax(if required)

Radiological finding

Lower lung field tuberculosis on chest X-ray was defined as the area lying below the horizontal arbitrary line drawn across the hila on the chest X-ray PA view. Para hilar region was considered in the lower lung fields and area above the line is upper lung field.¹⁵

Result

1. Age wise distribution

Age group	No.	%
\leq 30 years	12	5.45
31-40	24	10.91
41-50	40	18.18
51-60	78	35.45
61-70	64	29.09
>70	2	0.91
Total	220	100.00

The maximum incidence of pulmonary TB was noted above the age of 50 years. The peak incidence was in the age group of 51 - 60 years-78 (35.45%) and 61-70 years- 64(29.09%).

2. Pie diagram showing age wise distribution of patients



Above chart shows 65% of patients were >50 years of age and 35% were \leq 50 years

3. Sex wise distribution of patients

Age group	Male		Fem	ale	Total		
	No.	%	No.	%	No.	%	
Adult(≤50 years)	58	26.36	18	8.19	76	34.55	
Elderly (>50 years)	96	43.18	48	21.81	144	65.45	

Above chart shows 70% of patients were male and 30% were female.

4. Distribution of symptoms according to age

Symptom	≤50	years	>50 y	years	Tot	al	Chi-	P-
	NO.	%	NO.	%	NO.	%	square	value
Cough	72	94.74	136	94.44	208	94.55	.0082	.927
Fever	70	92.11	128	88.89	198	90	.57	.44
Haemoptysis	22	45.84	26	18.05	48	21.81	3.45	.06
Dyspnoea	22	28.95	74	51.39	96	43.64	10.18	.001
Anorexia	38	50	78	54.17	116	52.73	.008	.92
Loss of Weight	40	52.63	72	50	112	50.91	.13	.71
Chest Pain	6	7.89	10	6.94	16	7.27	.06	.79
Night Sweats	12	15.79	26	18.06	38	17.27	.17	.67

2019

The predominant symptoms noted were cough (94.55%), fever (90%), and anorexia (52.73%). Other symptoms noted were loss of weight (50.91%), dyspnoea (43.64%), haemoptysis

(21.81%), night sweats (17.27%) and chest-pain (7.27%). Prevalence of dyspnoea (significantly higher, p-value 0.0014) in elderly patients (age >50 years).

Symptom MALE FEMALE TOTAL Chi-P-NO. % NO. value NO. % % square Cough 146 94.80 93.93 208 94.54 .06 .79 62 134 87.01 96.96 198 90 5.08 .02 Fever 64 22.07 14 21.21 48 21.81 .02 .88 Haemoptysis 34 Dyspnoea 66 42.85 30 45.45 96 43.64 .12 .72 Anorexia 76 49.35 40 60.60 116 52.73 2.3 .12 Loss of Weight 72 46.75 40 60.60 112 50.91 3.54 .05 Chest Pain 7.27 10 6.49 6 9.09 16 .46 .49 Night Sweats 24 15.58 14 21.21 38 17.27 1.02 .31

5. Distribution of symptoms according to gender

The prevalence of fever significantly higher (p-value .02) in female patient.

6. Distribution of radiological pattern according to age

Chest X-ray Diagnosis	≤50 years		>50years		Total	
	NO.	%	NO.	%	NO.	%
Parenchymal opacity	2	2.63	12	8.33	14	6.36
Parenchymal opacity & Nodules	6	7.89	6	4.17	12	5.45
Nodules	12	15.79	14	9.72	26	11.81
Cavity	10	13.16	18	12.50	28	12.79
Cavity&Nodules	32	42.11	48	33.33	80	36.36
Cavity&consolidation	4	5.26	10	6.94	14	6.36
Consolidation	6	7.89	20	13.89	26	11.81
Fibrous cavity	2	2.63	4	2.78	6	2.72
Fibrosis	0	0.00	4	2.78	4	1.81
Bronchiectasis	0	0.00	4	2.78	4	1.81
Normal	2	2.63	4	2.78	6	2.72
Total	76	100	144	100	220	100

Chest x-ray showed cavity with nodular lesion in 36.36 %, cavity in 12.79% of the patients and nodular lesion in 11.81% of the patients. Other lesions noted are consolidation (11.81%), cavity with consolidation in 6.36%, parenchymal opacity

(6.36%), parenchymal opacity with nodule in(5.45%), fibrosis with cavity in (2.72%), fibrosis in(1.81%), bronchiectasis (1.81%) and 2.72% patients had normal chest x-ray.

7. Lung field involvement according to age

Lung field involvement	≤50	years	>50	years	Total		
Lung neid mvorvement	NO.	%	NO.	%	NO.	%	
Isolated upper lung field	30	39.47	38	26.39	68	30.90	
Isolated lower lung field	10	13.16	36	25.00	46	20.91	
Multiple lobe involvement	34	44.74	66	45.83	100	45.45	
Normal	2	2.63	4	2.78	6	2.73	
Total	76	100	144	100	220	100	
Chi-square=6.11 df=3 p-value=0.106							

Multiple lobe involvement is most common 100 (45.45%) followed by isolated upper lung field

68(30.90%) and then by isolated lower lung field 46(20.91%).

Radiological	<50years		>50	years	Total			
involvement	NO.	%	NO.	%	NO.	%		
Right	16	21.05	44	30.55	60	27.27		
Left	26	34.21	24	16.67	50	22.73		
Bilateral	32	42.10	72	50	52	47.27		
Normal	2	2.64	4	2.78	6	2.73		
Total	76	100	144	100	110	100		
Chi-square=40.3 df=3 p-value=0.000								

8. Analysis of side of lesion according to age

Overall bilateral involvement (47.27%) is most common followed by right sided involvement (27.27%) then by left sided involvement (22.73%) and 2.73% of patients have normal chest x-ray.

9. Radiological pattern of lower lung field tuberculosis



Lower lung field involvement was noted in 20.90% of patients. Chest x-ray of lower lung field shows consolidation in (39.14%), cavity with

nodule (17.39%), cavity in (13.05%), parenchymal opacity in (8.69%), nodules (8.69%) and bronchiectasis in 4.35%.



Diabetic TB patients were having sputum positivity 1+ in 39.09%, 2+ positivity in 10%, 3+ positivity in 22.73%, scanty in 14.55%, negative in 13.63% and BAL fluid positivity in 0.90% of

patients. Over all scanty or 1+ positive sputum (53.64%) was more common in patient with diabetes and pulmonary TB than 2+ or 3+ (32.73%).

Discussion

A clinical and radiological evaluation of 220 cases of pulmonary tuberculosis with diabetes mellitus was done. In our study the total number of males were 70% and females were 30%. The male to female ratio was 2.3:1. Other studies have shown that, the prevalence as well as incidence of tuberculosis is higher among males than among females. Patel Anand K et al (2012)⁷ found 73.6% male and 26.4% female, male to female ratio was 2.8:1. Hariprasad et al (2013)⁹ found 72% male and 28% females. The male to female ratio was 2.6:1. Chaya B E et al (2015)¹¹ found 72% males and 28% female, male to Female ratio was 2.5:1.Nilofer Shaikh et al (2016)¹² found 70% male and 30% females ,male to Female ratio was 2.3:1 Present study has similar male to female ratio as found in the study done by Nilofer Shaikh et al (2016).¹² The high incidence of disease in males is possibly due to the fact that both tuberculosis and diabetes are more common in males. Another reason could be that the number of male patients seeking medical attention or evaluation is more than females.

In the present study, maximum incidence of pulmonary TB was noted above the age of 40 years. The number of patients above 50 years were 65.45%. The peak incidence was seen in the age group of 51 - 60 years and 61-70 years. Hariprasad et al (2013)⁹ founded number of patients above the age of 40 were 79% and peak incidence was in the age groups of 40 - 49 and 60- 69 years. Chava et al $(2015)^{11}$ founded the number of patients above the age of 50 were 60% and peak incidence was in the age groups of 51-60years and 61-70years. Nilofer Shaik et al $(2016)^{12}$ founded maximum incidence of pulmonary TB was noted above the age of 40 years. The peak incidence was in the age group of 41 - 50 years and > 60 years. **C Babu Anand et** al (2017)¹³ founded the maximum incidence of pulmonary tuberculosis was reported above the age of 40 years. The peak incidence of pulmonary tuberculosis was reported in the age group of 41-50 and 51-60 years. Present study age distribution

correlate with study done by **Chaya et al (2015).**¹¹ Reason might be general morbidity increase with age, and progressive waning off of immunity with age.

The predominant symptoms noted in our study was cough (94.55%), fever (90%) and anorexia (52.73%) in both patients less than 50 years and more than 50 yrs. Prevalence of fever, chest pain and haemoptysis was higher in young adults (age < 50 years) while prevalence of dyspnoea were found significantly higher (p value < 0.0014) in elderly patients (age >50 years). which was comparable with the study by **Patel Anand K et** al $(2012)^7$ which shows most common symptoms of tuberculosis were cough (100%), fever(78.95%) and dyspnoea was significantly higher in patient >50 years. Nilofer Shaik et al (2016)¹² also reported three most common symptoms were cough (74.29%), fever (64.29%), and anorexia (77.14%). Surva Kant et al (2013)¹⁰ reported cough (87.61%), breathlessness (76.195%), fever (75.23%) as most common symptom among tuberculosis and diabetes mellitus group. Chaya B **E et al** $(2015)^{11}$ also reported the similar result of three most common symptoms cough (92%), fever (80%) and anorexia (58%).C. Babu Anand et al $(2017)^{13}$ noted anorexia in (81.7%), cough in (80%), followed by fever in (60%) of patients.

Cough is common because many are smokers which can be a contributing factor during disease process and fever may be due to host immune response to bacteria and could be due to auto immune response to maintain thermoregulatory system. Anorexia is because many patients are having less immunity or toxaemia, no proper nutritional diet. Dyspnoea was significantly higher in patient >50 years because most of them were smoker.

Present study shows overall sputum positivity of 86.37%. Overall sputum positivity reported by **Nilofer Shaikh et al (2016)**¹² was 62.85%. **Hariprasad et al (2013)**⁹ reported sputum positivity of 58%. **C. Babu Anand et al (2017)**¹³ reported 100% sputum positivity. Present study shows high sputum positivity due to more of

2019

cavitary lesion which maintains high bacterial population. Diabetic TB patients were having sputum positivity 1+ in 39.09%, 2+ positivity in 10%,3+ positivity in 22.73%,scanty in 14.55%, negative in 13.63% and BAL fluid positivity in 0.90% of patients.

In our study, right sided lesion was noted in 27.27% and left side in 21.21% and 47.27% of the lesions were bilateral. Bilateral and right sided lesion were significantly higher in patient age >50vears (p-value=0.000). Hariprasad et al (2013)⁹ reported study right sided lesion in 37% and left side in 33% and 30% were bilateral. Nilopher Shaikh et al (2016)¹² reported right sided lesion in 38.57% and left sided in 27.14% and rest (34.28%) of the lesions were bilateral. C Babu Anand et al (2017)¹³ reported right-sided lung lesions in 42% of the cases and left-sided lesions in 27% of the cases and bilateral lesion in 30%. The increased incidence of bilateral disease is due to the rapid dissemination of tuberculosis in diabetics. The increased incidence of right sided disease is probable due to more lung mass on the right side.

Our study shows multiple lobe involvement (45.45%) predominate than isolated upper lung field(30.90%) or isolated lower lung field (20.91%) which is comparable with study done by **S. Carreira et al (2012)**⁸ who reported multiple lobe involvement in (72.3%), isolated upper lung field in(17.1%) or isolated lower lung field in(10.6%).

Isolated lower lung field and multilobar involvement were higher in male and patient age more than 50 years.

Multiple lobe involvement due to rapid dissemination of tuberculosis in diabetics. Upper lung field involvement because alveolar concentration is more than arterial concentration in upper lung field and also bacteria being aerophilic grow better in upper lung field.

Overall pattern of lesion noted cavity with nodule in 36.36%, cavity in 12.79% and nodules in 11.81% of the patients. Other lesions noted are consolidation (11.81%), cavity with consolidation

(6.36%), parenchymal opacity with nodules (5.45%), fibrous cavity (2.72%), fibrosis(1.815), bronchiectasis (1.81%) and normal x-ray in 2.72%. In patients >50 years, cavity with nodule (33.33%) were the most common type of lesions noted followed by consolidation (13.89%), cavity (12.50%). In patients < 50 years, also cavity with nodule was more common (42.11%) followed by nodule (15.79%). Higher prevalence of cavities tuberculosis among pulmonary patients is probably because it causes extensive caseousnecrosis. Uncontrolled hyperglycaemia is a contributory factor for cavitary lesion. Nilofer sheikh et al 2016)¹² reported Overall cavitary lesions (52.88%) were the most common type of lesions noted followed by fibrosis (30%), and infiltration (27.14%) in both the age groups. In patients >50 years, cavitary lesions (64.86%) were the most common type of lesions noted followed by fibrosis (35.13%), infiltration (21.33%). In patients < 50 years, also cavitations was more common (45.45%) followed by infiltration (33.33%). Fibrosis (24.24%).

Consolidation (39.14%) was the most frequent finding on chest X-ray in LLFTB cases in our study.

Conclusion

- In the study group, 70% were males and 30% were females and the male to female ratio was 2.3:1.65.46% of the patients were above the age of 50 years.
- The predominant presenting symptoms noted were cough (94.55%), fever (90%) and anorexia (52.73%). Significant percentage of patients had loss of weight (50.91%) and dyspnoea (43.64%).
- Multiple lobe involvement present in 45.45% of the patients, isolated upper lung field in 30.90%, isolated lower lung field in 20.91% and right sided lesions were noted in 27.7% of cases, left sided in 22.73% and 47.27% had bilateral tuberculosis.
- Cavity with nodular lesions (36.37%) were the most common type of pattern noted.

2019

Radiological examination shows 43.63% had moderately advanced.

• Isolated lower lung field tuberculosis was noted in 20.91% of cases. Consolidation was most common pattern in lower lung field tuberculosis.

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2019

Abbreviation

TB-Tuberculosis DM-Diabetes mellitus RBS-Random blood sugar FBS-Fasting blood sugar PPBS-Post prandial blood sugar ULF-Upper lung field LLF-Lower lung field MTB-Mycobacterium tuberculosis Anti-TB-Antituberculosis DM-TB-Diabetes mellitus-Tuberculosis AIDS: Acquired immune deficiency syndrome HIV: Human immunodeficiency virus ATT: Antituberculosis therapy MDR-Multi drug resistant SPSS-Statistical package for the social sciences BAL-Bronchoalveolar lavage AFB-Acid fast bacilli LLFTB-Lower lung field tuberculosis